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## **REMARKS**

### **Status of Claims**

Claims 1, 2, 5, 7-21, and 23, 25-30 are pending. Claims 10-19 and 28-30 are withdrawn from consideration. Claims 1-2, 5, 7-9, 20, 21, 23 and 25-27 have been rejected. Claims 1, 9, 20 and 27 have been amended. Support for claim amendments can be found throughout the specification, for example, in paragraphs 0040, 0041, 0048, 0056, 0086, 0087, 0095, 0129 and 0131.

## **CLAIM REJECTIONS**

### **35 U.S.C. § 112 Rejections**

In the Office Action, the Examiner rejected claims 1-2, 5, 7-9, 20-21, 23, 25-27 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

The Examiner alleged that there is no original descriptive support for the phrase "virulence is stabilized". The Examiner further alleged that the specification does not teach or describe the phrase and as a result the claims recite new matter.

Applicants disagree. Support is provided in the specification in Figure 2. Figure 2 shows a measure of virulence and the figure demonstrates that after the 2<sup>nd</sup> passage there is a stabilization of virulence. A skilled artisan would readily deduce that since there's no increase in virulence after the 2<sup>nd</sup> passage, then virulence has been stabilized. Moreover, It is well established that, under proper circumstances, drawings alone may provide a written description of an invention as required by §112. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1564 (Fed. Cir. 1991). Further, MPEP 2163.03 also states: "The subject matter of the claim need not be described literally (i.e., using the same terms or in haec verba) in order for the disclosure to satisfy the description requirement." Hence, sufficient description is provided by the specification.

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In the office action, the Examiner rejected claims 1-2, 5, 7, 9, 20-21, 23, 25, 27 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement.

The Examiner alleged that the term “animal” recited in the claims is defined to include humans and that harvesting organs from a living human would not be permitted in the United States.

Applicants disagree. Claims have been amended to recite harvesting from a non-human animal, therefore the rejection is moot in light of the claim amendments. Hence, Applicants request withdrawal of the claim rejections.

### **35 U.S.C. § 103 Rejections**

In the Office Action, the Examiner rejected claims 1-2, 5, 7-9, 20-21, 23, 25-27 under 35 U.S.C. § 103(a), as allegedly being unpatentable over Pawelek (US Patent 6,685,935) in view of Vahidy et al (1996, reference cited on USPTO 1449) [“Vahidy”] and Pan et al (1995, reference cited on USPTO 1449) [“Pan”].

The Examiner alleged that Pawelek teach the claimed methods and therefore produce strains of bacterial vaccine vectors that would have the same or equivalent functional characteristics based upon equivalent method steps that recite successive administration, passage and harvesting of the bacterial vaccine vectors to achieve “super infective” bacterial strains. However, Pawelek fails to show the selection of a *Listeria* bacterial vaccine vector that expresses a tumor heterologous antigen recombinantly expressed by a maximum load selected *Listeria* vector. Vahidy allegedly teaches a maximum load selection process for animal passaged *Listeria monocytogenes* (Lm) that results in increased viability counts per gram of infected organ where each passage corresponds to infectivity and virulence operon activation. The Examiner further alleged that Pan showed that the recombinant *Listeria monocytogenes* (Lm) induced a cell-mediated immunity against the antigen. Therefore, the Examiner alleged that it would have been obvious to carry out the maximum load selection process taught by Vahidy for the *Listeria monocytogenes* (Lm) vaccine vector as taught by

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Pawelek because Vahidy teach that through animal passage of Lm, the count per gram of infected organ increases to maximum load levels which would provide for stimulation of an enhanced immune response to an encoded heterologous antigen as taught by Pan or Pawelek.

Applicants disagree. The combination of Vahidy, Pawelek and Pan teach away from the claimed invention. The claims are directed, *inter alia*, to harvesting a Listerial vaccine vector from a normal organ or normal tissue (emphasis added), "...until a maximum bacterial load for said vector in said organ or tissue is reached and virulence of said vector is stabilized". Pawelek does not disclose reaching a maximum bacterial load in normal tissue but rather aims to build a vector that is "super-infective" for tumor tissue, as the Examiner asserts throughout the Jan. 26, 2011 Office Action. Therefore, a skilled artisan when combining Vahidy, with the methods of Pawelek and Pan would be led to carry out the claimed methods in tumor cells selectively as opposed to doing so in normal tissue or organs. Hence, whereas Pawelek relates to bacterial growth and selection in tumors, to the contrary, the present invention selects for growth in normal tissue in order to maximize the potential to grow in normal tissue. The present invention further prevents one practicing the invention to from administering a bacterial vaccine vector that has the possibility to increase virulence in human beings and it further provides a process that enables stable and safe usage of a vaccine vector in humans, (as evidenced in Figure 2) wherein the vaccine vector serves to enhance the immunogenicity to a heterologous antigen expressed thereby.

Moreover, the combination of Vahidy, Pawelek, and Pan does not set forth all of the claimed elements of the present invention since, as noted above, the combination of the cited references would lead to a skilled artisan practicing methods disclosed therein in tumor cells, since Pawelek teaches vectors that are "super-infective" for tumor cells and hence do not increase and stabilize virulence in normal tissue. Hence, for these same reasons a skilled artisan would not be motivated to arrive at the claimed invention.

In view of the foregoing amendments and remarks, Applicants assert that the pending claims are allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone

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number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 50-3355.

Respectfully submitted,

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